IN THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant: Sheng-Ping Zhong

Serial No.: 10/667,151

Filed: 09/18/2003

Title: INJECTABLE THERAPEUTIC FORMULATIONS

Art Unit: 1611

Examiner: Charlesworth E. Rae

Confirm. No.: 8726

Docket No.: 03-151US1

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APPEAL BRIEF UNDER 37 C.F.R. §41.37

Sir:

Appellant filed a Notice of Appeal and a Request for Pre-Appeal Brief Review on December 1, 2008. An Appeal Brief was duly filed on March 2, 2009. In response, the Examiner did not file an Examiner's Brief and, instead, opted to reopen prosecution of the case (removing it from appeal) and issued a non-final office action on June 23, 2009, to which the Applicant could file a response or initiate a new appeal by filing a notice of appeal. Appellant subsequently filed a Notice of Appeal on December 21, 2009. An Appeal Brief was due February 21, 2010. Appellant unintentionally failed to timely file an Appeal Brief. Appellant submits this Appeal Brief concurrently with a Petition for Revival of an Application For Patent Abandoned Unintentionally Under 37 CFR 1.137(b). The Office had previously acknowledged that the previously paid Appeal Brief fee of $540 would be applied to a new appeal. Thus, the Office is hereby authorized to apply the previously paid fee as set forth in §41.20(b)(2) ($540) to the instant Appeal. The Office is authorized to charge any other fees deemed to be due or credit for any excess may be directed to Deposit Account 50-1047.

Appellant respectfully requests that the Board of Patent Appeals and Interferences reverse the Examiner's rejection of the claimed subject matter.

I. REAL PARTY IN INTEREST

Scimed Life Systems, Inc. is the assignee of the present invention and the real party in interest.

II. RELATED APPEALS AND INTERFERENCES

No other appeals or interferences within the meaning of 37 C.F.R. § 1.912(c) are known to Appellant's legal representative, or the assignees, which will directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

The claims in this application are claims 1-39.

Claims 22-37 were withdrawn from consideration pursuant to a restriction requirement.

Claims 1-21, 38 and 39, the subject of this appeal, were finally rejected and are provided in the attached Appendix.

Appellant hereby appeals the final decision of the Examiner in the above-identified application rejecting claims 1-21, 38, and 39.

IV. STATUS OF AMENDMENTS

A Final Office Action was mailed on June 9, 2008, rejecting claims 1-21, 38, and 39. A Notice of Appeal and response to the Final Office Action was filed on December 1, 2008, and in an Advisory Action mailed on December 30, 2008, the Examiner indicated that the request for reconsideration was considered but did not place the application in condition for allowance.

An Appeal Brief was filed on March 2, 2009. In response, the Examiner reopened prosecution of the case and issued a non-final office action on June 23, 2009. Appellant subsequently filed a second Notice of Appeal on December 21, 2009.

The claims have not been amended subsequent to the final rejection.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention provides injectable formulations for chemoablation of tissue. The formulations combine a chemical ablation agent in an amount effective to cause tissue necrosis with a biodisintegrable viscosity adjusting agent to render the formulations highly viscous.

The invention is described in claim 1, the sole independent claim under appeal. Claim 1 is drawn to an injectable formulation comprising: (a) a chemical ablation agent in an amount effective to cause tissue necrosis, and (b) a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous, wherein said injectable formulation is a sterile injectable formulation.

The claimed invention provides advantages relative to the prior art (*see* specification, paragraph [0011] to [0015].

One advantage of the invention is that the formulations have improved retention in prostatic and other tissue, thereby improving delivery efficiency while minimizing adverse effects such as nonspecific damage caused by the chemical ablation agent.

Another advantage is that the injectable formulations that are capable of being injected into tissue using conventional syringes, injection catheters, and so forth, even though once injected, they have good retention in tissue.

Yet another advantage is that the injectable formulations provide controlled release of chemoablative agents.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following grounds of rejection are presented for review:

Rejections under 35 U.S.C. 103(a) - Escandon et al.

Claims 1-6, 11-12, and 20-21 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon et al. (US Pub. No. 2003/0092689, "Escandon").

Claims 9-10, 13, and 19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Ramstack et al. (U.S. Patent No. 6,667,061, "Ramstack").

Claims 7-8 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon, in view of Ramstack, and further in view of Lund (U.S. Patent No. 3,869,546, "Lund").

Claims 14 and 16-18 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Glajch et al. (U.S. Patent No. 5,147,631, "Glajch").

Claim 15 is rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Lauffer et al. (U.S. Patent No. 7,175,829, "Lauffer").

Claims 38-39 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Cochrum (U.S. Patent No. 5,614,204, "Cochrum").

VII. ARGUMENT

The following legal authorities are relied on in the following argument in the order in which they are cited:

In re Rijckaert, 9 F.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993).
In re Oelrich, 666 F.2d 578, 581-82, 212 U.S.P.Q. 323, 326 (CCPA 1981).
In re Robertson, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999).
MPEP 2112 IV.
MPEP § 2142.
In re Eli Lilly & Co., 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990).
MPEP 2141.02.

Akzo N.V. v. International Trade Commission, 808 F.2d 1471, 1480-81, 1 U.S.P.Q.2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909 (1987), *Loctite Corp. v. Ultraseal Ltd.,* 781 F.2d 861, 874, 228 U.S.P.Q. 90-99 (Fed. Cir. 1985).
In re Clay, 966 F.2d 656, 23 U.S.P.Q.2d, 1058, 1060 (Fed. Cir. 1992).
In re Jones, 958 F.2d 347, 351, 21 U.S.P.Q.2d 1941, 1943-44 (Fed. Cir. 1992).
In re Fine, 837 F.2d 1071, 1075, 5 U.S.P.Q. 1596, 1598-99 (Fed. Cir. 1988).

The References

Escandon et al.

Escandon teaches a treatment regimen for treating diseased prostate tissue. This treatment regimen, as repeated throughout Escandon, consists of the ***co-administration*** of ethanol and an antiandrogen (*see, e.g.,* paragraphs [0031], [0032], [0033], [0042]). Specifically, Escandon teaches injection of liquid ethanol into the prostate ("injection of ethanol (absolute alcohol) into the prostate to be treated") (Escandon, paragraph [0044]), using a PROSTAJECT surgical device for "chemically ablating prostate tissue sufficiently to elicit a reparative process in the absence of further treatment; and coadministering a therapeutically effective amount of an antiandrogen." (Escandon, paragraph [0042]). Escandon teaches that a gelling agent may be added as an additive.

Ramstack et al.

Ramstack teaches "injectable compositions having improved injectability, and to methods for the preparations of such injectable compositions." For example, Ramstack teaches "dry microparticles [that] are mixed with an aqueous injection vehicle to form a first suspension [and] [t]he first suspension is mixed with a viscosity enhancing agent to form a second suspension." (Ramstack, col. 3, lines 37-41). Ramstack does not teach a chemical ablation agent. Ramstack does not teach an injectable formulation for chemical ablation of any type.

Lund

Lund teaches "[s]olutions of…therapeutic mixture[s] [that] have viscosities which are lowered to the point where they can be utilized commercially in a practical manner, while at the same time retaining the favorable adjuvant effects." (Lund, Abstract). Lund does not teach a chemical ablation agent. Lund does not teach an injectable formulation for chemical ablation of any type. Lund teaches that polymers including "Carbopol cross-linked acrylic acid polymers would be most desirable if the high viscosity of useful ranges did not render it impracticable in formulation and dispensing operations." (Lund, col. 2, lines 14-18).

Glajch et al.

Glajch et al. teaches ultrasound contrast agents made of porous particles of an inorganic material containing an entrapped gas or liquid and having an average particle diameter of about 0.05 to 500 microns, and selected from one or more of the group consisting of: monomeric or polymeric borates; monomeric or polymeric aluminas; monomeric or polymeric carbonates; monomeric or polymeric silicas; and monomeric or polymeric phosphates; and pharmaceutically acceptable organic or inorganic cationic salts thereof. Glajch et al. does not teach an injectable formulation of any type for chemical ablation of tissue.

Lauffer

Lauffer et al. teaches a method for contrast-enhanced diagnostic imaging using contrast agents capable of binding to a targeted tissue or tissue component. The use of contrast agents allow for "real-time" monitoring during thermal interventional therapy of thermally-induced necrosis. Lauffer does not teach an injectable formulation of any type for chemical ablation of tissue. Lauffer does not teach chemical ablation of tissue.

Cochrum

Cochrum teaches vascular occlusion agents such as "[s]urgical gelfoam, a solid slowly absorbed gelatin, probably…the most widely used embolic agent today…A primary disadvantage of Gelfoam is that it has to be injected in solid foam form."

Cochrum does not teach any chemical ablation agents. Cochrum does not teach combining a chemical ablation agent with a viscosity adjusting agent.

The Rejections Under Appeal

Rejection Under 35 U.S.C. §103(a) over Escandon et al.

Claims 1-6, 11-12, and 20-21 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon et al. (US Pub. No. 2003/0092689, "Escandon").

The rejection over Escandon is erroneous. The Examiner has failed to meet his burden of establishing how Escandon teaches or suggests each and every element of the claimed invention. The invention of claim 1 is directed to an injectable formulation comprising: (a) a chemical ablation agent in an amount effective to cause tissue necrosis, and (b) a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous, wherein said injectable formulation is a sterile injectable formulation.

In the Office Action dated June 23, 2009, the Examiner states that it would have been obvious to prepare a sterile injectable ablation formulation comprising ethanol and GELFOAM® as taught in Escandon. The Examiner states that "GELFOAM is a gelatin powder and therefore reads on the term "a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous."

To support this assertion, the Examiner makes the assumption that "Gelfoam is a gelling agent [so] one would reasonably expect that chemoablation fluids comprising Gelfoam would be rendered highly viscous because gels are known in the art to be highly viscous when compared to conventional liquid formulations."

Appellant states that the purported equivalence between GELFOAM and the claimed element has not been established. Appellant respectfully states that nowhere within the four corners of Escandon is there a claim that GELFOAM® is a biodisintegrable viscosity adjusting agent or equivalent to a "biodisintegrable viscosity adjusting agent." Indeed, the terms "viscous" or "viscosity" or "viscosity adjusting agent" ***do not appear anywhere*** within the four corners of Escandon. The Examiner himself has provided no evidence to support his assumption but merely states out of hand

that "gels are known in the art to be highly viscous when compared to conventional liquid formulations."

Appellant respectfully submits that the Examiner appears to be making an inherency argument but without the requisite proof. Appellant respectfully states that a proper inherency argument cannot be based solely upon the Examiner's unsupported assertion and assumption. Indeed, the law is clear that a holding of inherency must flow as a necessary conclusion from the prior art, not simply a possible one. The fact that a certain result or characteristic ***may*** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 U.S.P.Q. 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted); MPEP 2112 IV.

Escandon clearly is missing any description of a "viscosity enhancing agent." The Examiner has not shown how this missing descriptive matter is necessarily present in the thing described in the reference and that it would be so recognized by persons of ordinary skill. Given that the Examiner has failed to provide any extrinsic evidence that GELFOAM® reads on the term "biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous," Appellant respectfully states that the Examiner has failed to meet his burden of showing how Escandon teaches or suggests each and every element of the claimed invention.

In addition to the fact that Escandon is missing a claimed element (i.e. a biodisintegrable viscosity enhancing agent), Appellant provides the following additional reason why the obviousness rejection fails. The obviousness rejection fails because the totality of the evidence teaches away from preparing the claimed injectable formulations. One of skill in the art would, in light of the totality of the disclosures of the prior art

references in the record, be taught away from preparing the claimed injectable formulation by mixing together a chemical ablation agent in an amount effective to cause tissue necrosis, and a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous.

Escandon et al. teaches that "GELFOAM is a gelatin powder consisting of particles in the 40-60 micron range and is commonly used as an ***embolizing agent***." (Escandon, paragraph [0063])(emphasis added). One of skill in the art would not read "embolizing agent" and be led to utilize the GELFOAM® as a viscosity adjusting agent. Appellant states that one of skill in the art would appreciate that an embolizing agent causes an obstruction or occlusion in a vessel and upon reading Escandon's description of GELFOAM® as an embolizing agent, would be taught away from utilizing the GELFOAM® as a viscosity adjusting agent that would be suitable for an injectable formulation since it may cause the chemical ablation agent to cause an obstruction or clog when utilized as an injectable formulation.

Indeed, Cochrum, which has been cited as a prior art reference, states the disadvantages of GELFOAM. Cochrum teaches that "Surgical Gelfoam, a solid slowly absorbed gelatin, probably is the most widely used embolic agent today…A primary disadvantage of Gelfoam is that it has to be injected in solid foam form. When the larger emboli are needed, the foam often blocks the catheter and a guidewire must be used to push and fragment the foam material. This may require strong force which may be dangerous since the generated force can cause the catheter tip to recoil and cause embolic reflux or the tip may cause vessel wall injury." (Cochrum, col. 2, lines 27-42).

Given these disclosures about GELFOAM as a solid, embolic agent, one of skill in the art would have no motivation to utilize GELFOAM as a biodisintegrable viscosity adjusting agent in the claimed injectable formulations.

Lund, which was also cited as a prior art reference, teaches that it is undesirable to have a viscous polymer such as Carbopol cross-linked acrylic acid polymers, in an injectable formulation. As a solution to this problem, Lund teaches a method to "lower substantially the viscosity of aqueous solutions of the polymers" (Lund, col. 2, lines 36-38) to "control[] the viscosity thereof to permit them to be readily mixed within an active agent and easily injected into a host." (Lund, col. 2, lines 21-23).

In making the obviousness rejection, the Examiner is required to consider the entire record and cannot dismiss the disclosures of the prior art reference or his own admissions regarding the prior art. Applicants respectfully state that the Examiner cannot pick and choose certain portions of the entire record in making a determination of obviousness. This particular rejection pertains to Escandon.

Appellant states that given the totality of the teachings of the record, one of skill in the art would not be motivated to combine the claimed chemical ablation agent with GELFOAM. Just as importantly, one of ordinary skill in the art would ***not*** have a reasonable expectation of success that utilizing an embolic agent in combination with a chemical ablation agent would result in the present invention.

As articulated in MPEP 2142, "When an applicant submits evidence, whether in the specification as originally filed or in reply to a rejection, the examiner must reconsider the patentability of the claimed invention. The decision on patentability must be made based upon consideration of ***all*** the evidence, including the evidence submitted by the examiner and the evidence submitted by the applicant. A decision to make or maintain a rejection in the face of all the evidence must show that it was based on the ***totality*** of the evidence. Facts established by rebuttal evidence must be evaluated along with the facts on which the conclusion of obviousness was reached, not against the conclusion itself," citing *In re Eli Lilly & Co.*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990)(emphasis added).

Appellant respectfully states that the teachings within Escandon as well as the other cited prior art would undermine a finding of obviousness. Appellant states that the totality of the evidence must be considered and certainly, "prior art must be considered in its entirety, including disclosures that teach away from the claims." MPEP 2141.02.

Appellant states that given Appellant's arguments, Appellant has effectively overcome the rejection by showing that Examiner has failed to establish that the "biodisintegrable viscosity adjusting agent" is provided in Escandon. In addition, Appellant states that the totality of the record shows that one of skill in the art would not be motivated to utilize GELFOAM in the manner of the claimed invention or have any reasonable expectation of success given the teachings of the prior art.

Given the above remarks, Applicant states that a *prima facie* case of obviousness has not been established and in the alternative, such *prima facie* case have been overcome with this rebuttal and respectfully requests that the Examiner withdraw the rejections. Claim 1 is an independent claim, and the above comments apply directly to it. All other rejected claims are dependent directly on claim 1 and the rejection of those claims fails at least because of the fundamental defect discussed above.

For at least these reasons, Appellant respectfully submits that claims 1-13, 19-21 and 38-39 and 38-39 are patentable over Escandon.

Rejection Under 35 U.S.C. §103(a) over Escandon in combination with various secondary references

Claims 9-10, 13, and 19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Ramstack et al. (U.S. Patent No. 6,667,061, "Ramstack").

Claims 7-8 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon, in view of Ramstack, and further in view of Lund (U.S. Patent No. 3,869,546, "Lund").

Claims 14 and 16-18 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Glajch et al. (U.S. Patent No. 5,147,631, "Glajch").

Claim 15 is rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Lauffer et al. (U.S. Patent No. 7,175,829, "Lauffer").

Claims 38-39 are rejected under 35 U.S.C. §103(a) as being unpatentable over Escandon in view of Cochrum (U.S. Patent No. 5,614,204, "Cochrum").

The rejected claims are all dependent upon independent Claim 1, and thus include all of the features of that claim together with the further claim features explicitly recited.

The deficiencies of Escandon have been discussed above. The cited secondary references do not remedy the deficiencies of Escandon. One of skill in the art would not reasonably expect to successfully arrive at the present invention given that Escandon teaches GELFOAM is an embolic agent. One would not be motivated to manipulate the formulations of Escandon to arrive at the claimed invention of these various dependent claims.

To make any of these combinations and make a conclusion of obviousness could only be based on the use of *undue* hindsight, which has long been held to be impermissible. *See Akzo N.V. v. International Trade Commission,* 808 F.2d 1471, 1480-81, 1 U.S.P.Q.2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909 (1987), *Loctite Corp. v. Ultraseal Ltd.,* 781 F.2d 861, 874, 228 U.S.P.Q. 90-99 (Fed. Cir. 1985).

To whatever extent one ***could*** combine the teachings of the two references, it is quite clear that the claimed viscous injectable formulation that causes tissue necrosis would still not be formed. Even with the use of impermissible hindsight, one of ordinary skill in the art would not have arrived at the present invention from a combination of the reference teachings. Just as important is the fact that there would be no motivation or suggestion to combine the references as the Examiner has done. *See In re Clay*, 966 F.2d 656, 23 U.S.P.Q.2d, 1058, 1060 (Fed. Cir. 1992), *In re Jones*, 958 F.2d 347, 351, 21 U.S.P.Q.2d 1941, 1943-44 (Fed. Cir. 1992), *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d, 1596, 1598-99 (Fed. Cir. 1988).

For at least these reasons, it is respectfully submitted that these claims, which all depend upon independent claim 1, are patentable over the cited references. The rejected claims depend upon claim 1 and are therefore patentable for at least the same reasons as is claim 1.

VIII. CONCLUSION

The references relied on by the Examiner do not support a *prima facie* case of obviousness. Thus, it is respectfully submitted that reversal of the rejections of record is in order.

IX. FEES

Appellant's undersigned representative hereby authorizes the Commissioner to charge any fees due and owing with respect to the filing of this paper to deposit account No. 50-1047.

Dated: December 31, 2010

Respectfully submitted,

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X. CLAIMS APPENDIX

1. An injectable formulation comprising: (a) a chemical ablation agent in an amount effective to cause tissue necrosis, and (b) a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous, wherein said injectable formulation is a sterile injectable formulation.

2. The injectable formulation of claim 1, wherein said ablation agent is an osmotic-stress-generating agent.

3. The injectable formulation of claim 1, wherein said ablation agent is an organic ablation agent.

4. The injectable formulation of claim 1, wherein said ablation agent is ethanol.

5. The injectable formulation of claim 1, wherein said ablation agent is a salt.

6. The injectable formulation of claim 1, wherein said ablation agent is sodium chloride.

7. The injectable formulation of claim 1, wherein said viscosity adjusting agent is present in an amount effective to provide a kinematic viscosity ranging from 5,000 cps to 100,000 cps.

8. The injectable formulation of claim 1, wherein said viscosity adjusting agent is present in an amount effective to provide a kinematic viscosity ranging from 10,000 cps to 50,000 cps.

9. The injectable formulation of claim 1, wherein said viscosity adjusting agent comprises a polysaccharide.

10. The injectable formulation of claim 9, wherein said viscosity adjusting agent is a polysaccharide selected from methylcellulose, hydroxyethylcellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, methylhydroxyethylcellulose, methylhydroxypropylcellulose, carboxymethyl cellulose and its salts, hydroxyethylcarboxymethylcellulose and its salts, carboxymethylhydroxyethylcellulose and its salts, alginic acid and its salts, hyaluronic acid and its salts, carageenan, chitosan, xanthan gum, guar gum, gum arabic, gum karaya , gum ghatti, konjac and gum tragacanth.

11. The injectable formulation of claim 1, wherein said viscosity adjusting agent comprises a polypeptide.

12. The injectable formulation of claim 11, wherein said viscosity adjusting agent is selected from gelatin and collagen.

13. The injectable formulation of claim 1, wherein said viscosity adjusting agent is selected from carboxyvinyl polymer, polyvinylpyrrolidone, polyacrylic acid, polyacrylamide, polyacilic acid/acrylamide copolymer, polyethylene oxide, polypropylene oxide, poly(ethylene oxide-propylene oxide), polymetaphosphate, polyethyleneamine, polypyrridine, as well as salts thereof.

14. The injectable formulation of claim 1, further comprising an imaging contrast agent.

15. The injectable formulation of claim 14, wherein the imaging contrast agent is an MRI imaging contrast agent.

16. The injectable formulation of claim 14, wherein the imaging contrast agent is an ultrasonic imaging contrast agent.

17. The injectable formulation of claim 16, wherein the ultrasonic imaging contrast agent comprises a plurality of solid particles.

18. The injectable formulation of claim 17, wherein the plurality of solid particles is selected from calcium carbonate particles, hydroxyapatite particles, silica particles, poly(lactic acid) particles, and poly(glycolic acid) particles.

19. The injectable formulation of claim 1, wherein said injectable formulation comprises a plurality of viscosity adjusting agents.

20. The injectable formulation of claim 1, wherein said injectable formulation comprises a plurality of ablation agents.

21. The injectable formulation of claim 1, wherein said injectable formulation further comprises a liquid selected from water and an organic solvent.

38. The injectable formulation of claim 1, wherein said injectable formulation comprises an ionically crosslinkable polymer.

39. The injectable formulation of claim 38, wherein said ionically crosslinkable polymer is an alginate polymer.

XI. EVIDENCE APPENDIX

None.

XII. RELATED PROCEEDINGS APPENDIX

None.